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EDITORIAL

DABBLING WITH DYESTUFFS

JOSEPH'S "coat of many colors" would hardly be noticed at Easter parade on Atlantic City's Boardwalk. Its colors of vegetable or animal origin would have been altogether too subdued to incite to attention. The coal tar chemist has gone so far ahead of nature in color command that natural colors are "not in it any more"—and little children of the slums wear clothes giddier with purples and pinks than ever graced the Queen of Sheba's wardrobe.

And the Easter parade at the gay seashore outshines, in variety and brilliance of colors, the most exotic tropic garden.

The peacock's feather, the glowing orchid, and the lurid wing of the monarch butterfly, despite their color ecstasies, are outdone in brilliance, and certainly in utility, by the sweat of grimy coal tar, modified by chemists.

In all its appeals to the senses, coal tar is just a mess, yet its chemical progeny can siren every sense, and outdo nature's proudest products in titillating man's esthetic tastes.

The red of Joseph's coat might well have been the red of Mrs Coccus Cacti, still used to color medicinals—the blue was from rotted indigo leaves, and the yellow—from jaundiced saffron.

But they were, as colors, drab and undependable.

Today, thanks to chemical research, there are tens of thousands of dyestuffs for every simple, natural dyestuff used a century ago, and they are faster to the elements and vastly higher in color value than their old-time relatives. Furthermore, they are as diversified in character and properties as they are single-tracked in ancestry—all claiming the crude parenthood of Old King Coal, the fossil fuel, father of a full five-million flock.

Not the least interesting, and certainly not the least important of their services, is their use in medicine as bacteriostatic and diagnostic

agents. Methylene blue, gentian violet, acriflavine, mercurochrome, and many others, serve as surgical antiseptics. Fuchsine, eosin, pyoktannin and others serve as bacterial stains. The phthaleins are useful diagnostic aids.

But there are several avenues of use for dyestuffs in pharmacy, which have been rather generally overlooked.

Certainly an oral wash colored with one or more of the harmless certified dyestuffs bespeaks a cleanlier and a more esthetic taste than a mouthwash colored red with insect carcasses—which is precisely the origin of cochineal, still often used for a color source.

Then, show bottles expensively and laboriously filled with colored chemicals in solution are much more brilliantly and much more economically colored with readily available dyestuffs. Every pharmacy sells packaged dyestuffs for the household, but seldom does it occur to the show-bottle filler that these dyestuffs are water soluble and instantly ready for use. Some of the medicinal dyestuffs may also be so used, although those of the basic group are not so fast to light.

Easter egg dyes, shoe colors, wood stains, and many such preparations may be readily and profitably prepared by the enterprising pharmacist, who knows his sources of information and studies well the properties and applications of this most diversified and useful group of all of coal tar's children.

IVOR GRIFFITH.

Vacuum-Packed Milk Kept Fresh 42 Days

Milk kept fresh for six weeks, by a new method of vacuum packing, promises to revolutionize the dairy industry, if the technique is generally adopted.

The new method will be described in *Food Industries,* by Howard T. Greene, general manager of a large Wisconsin dairy firm that supplies the Milwaukee market.

The milk is put into ordinary milk bottles, but a tight metal cap with a gasket is used instead of the ordinary paper cap. Just before the cap is lowered into place and pressed home, live steam is introduced over the top of the milk. After the cap is sealed on, the steam is condensed, creating a partial vacuum.

Thus sealed, the milk will remain fresh for forty-eight hours at ordinary temperatures, or for six weeks if suitably refrigerated.—(*Science News.*)

ORIGINAL ARTICLES

BUILDING CASTLES OF HEALTH

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(*Continued from September Issue*)

BACTERIOLOGICAL EXAMINATIONS IN CASES OF DIPHTHERIA

Cultures, when properly made from throats and nasal passages and after careful examinations by experienced workers reveal diphtheria bacilli, are a means of supplying valuable information. The detection of true diphtheria bacilli in apparent healthy individuals reveal the latter as "carriers".

In suspicious sore throats, it is important to emphasize the fact that cultures though essential and very valuable will not present all of the information necessary to determine the gravity of the case or even as much as is given by the definite and prevailing clinical appearances. The finding of few diphtheria bacilli by bacteriological methods in a suspicious sore throat does not NECESSARILY signifiy clinical diphtheria. The sore throat may be due to another organism and the finding of few diphtheria bacilli may be significant of the fact that one is dealing with a carrier. When cultures reveal few diphtheria bacilli, the presence or absence of frank clinical manifestations (clear clinical signs of diphtheria) are the more important guides for regarding a case as clinical diphtheria. If under such conditions there is any question of doubt, it is best to resort to specific treatment, to inject antitoxin; in other words it is best to be safe than sorry.

It is well to remember that clinical diphtheria does not occur without the presence of diphtheria bacilli in the affected area. There have been typical cases of diphtheria in which, however, bacilli were not found in the cultures. Such reported absence of bacilli in cultures must be regarded of import only in proportion to the skill with which the cultures were made, the swab may not have actually touched the pseudo-membrane or exudate, an unsatisfactory tube of culture medium may have been employed, the inoculated tubes may have been carried around for many hours under unfavorable conditions before being properly incubated, or there may be some question as to the

actual knowledge and satisfactory experience of the one who examined the cultures. In many of these cases, later cultures revealed diphtheria bacilli. It is not advisable to wait for a laboratory report after taking cultures for a bacteriological examination before deciding as to the next step. Valuable time may be lost, for before the lapse of the sixteen to twenty-four and more hours required for the findings of the laboratory report, the extent of the disease improves or gets worse, thus usually allowing a prognosis. The intelligent and careful physician knows how to employ advantageously laboratory findings. If after taking cultures in suspicious sore throats, the diagnostician proceeds immediately to administer antitoxin, being guided by the clinical history and physical findings, he suspects clinical diphtheria and is treating the case in the most modern scientific manner. No harm has been done by the injection if the result of the laboratory examination is negative; but if the latter is returned positive, much time has been gained in treatment and possibly a life has been saved. It is of interest to note that the need for bacteriological examinations in suspected cases of diphtheria aided in the establishment of diagnostic laboratories. In New York City there was founded the first diagnostic laboratory where Dr. Biggs in 1893 offered the assistance of laboratory aids in the diagnosis of diphtheria.

TOXIN

As far back as 1884, Löffler and other early workers in diphtheria suspected and assumed that, in part at least, the harmful effects of the bacilli causing this infection were due to a poison (diphtheria toxin) elaborated by the organisms. It was in 1888 that Roux and Yersin, two pupils of Louis Pasteur the eminent French scientist, revealed the actual existence of such a toxin when they definitely proved that the diphtheria bacilli produce a soluble toxic substance. They grew the organisms in broth cultures, removed the former from the culture fluid by filtration through a Chamberland filter and found that the liquid which passed through (the filtrate) free of bacilli was toxic for guinea pigs. It is this toxin free of the bacilli (and therefore known as an extracellular or soluble toxin) which in diphtheria ordinarily does most of the damage; and it is the toxin which must be combated, when diphtheria infection prevails in human beings. William Henry Welch (1850-1934) of Johns Hopkins University and Simon Flexner (1863-), now of the Rockefeller Institute demonstrated the abnormal changes produced experimentally by injections of diphtheria toxin (1891-92), this work being con-

ducted simultaneously with that of Emil von Behring (1854-1917), professor of hygiene at Halle and later at Marburg. Today considerable information is available concerning the action of diphtheria toxin upon body tissues, its selective action upon certain nerve centers, and finally to the late degeneration of the heart muscle which is the cause of postdiphtheritic death.

May I assure you that diphtheria toxin is not an imaginary product. In fact it is possible to produce as large amounts as may be needed. It is true that the EXACT chemical composition of such commercially prepared toxin is not definitely known. On the other hand, much is known of its stability, behavior toward chemicals and physical agents, and its reactions after it is injected into animals. Methods have been developed of measuring the degree of toxicity or potency of toxin in terms of the fundamental unit of toxicity. This is the M. L. D. or minimal lethal dose or the smallest amount of toxin which after subcutaneous (beneath the skin) injection kills a guinea pig weighing 250 grams on the fourth day. The production of a potent toxin is of great import today, for this becomes the starting point for the manufacture of all of the other preparations employed in the prevention and treatment of diphtheria.

DIPHTHERIA ANTITOXIN

In the production of artificial remedies to combat or prevent disease, science employs most frequently techniques simulating Nature's own process of developing such valuable agents. In diphtheria, our systems produce antidotes or neutralizers (or antibodies) which attempt to neutralize or render harmless the poison or toxin given off by the invading diphtheria bacilli. It is by means of these antibodies, the mobilization of troops, that the progress of disease can be retarded. The greater the number of troops, which means the more the antibody content and the more rapid the mobilization, that is the quicker these antibodies are produced, the more assured will be the quick return to normal health. The bacteria would thus be unable to become entrenched and gain the upper hand. When the antibodies are specific for the neutralization of toxin, they are most frequently spoken of as antitoxic bodies or antitoxin.

Emil von Behring demonstrated that animals could be treated with diphtheria toxin prepared in the laboratory, with the result that the serum of the blood of animals could be made to yield large quantities of diphtheria antitoxin. This serum could then be used in the

treatment of and as a temporary preventive remedy against diphtheria in human beings due to the specific neutralization of the toxin produced by the bacilli. In 1894, large scale production of diphtheria antitoxin was started by various commercial houses so as to make available this specific remedy for the scourge diphtheria. In December of the same year, the *New York Herald* antitoxin fund was turned over to the New York City Health Department. The following year the latter bureau began to make, distribute and administer this remedy. Some cities and state health departments followed their example. Today but few of these governmental departments actually make the diphtheria antitoxin, as they have found it is cheaper and more convenient to purchase the marketed product; but most of them distribute this as well as other biological products of value in the cure or prevention of disease.

The methods for producing diphtheria antitoxin commercially vary only in minor technical details. The first step for successful antitoxin production is obtaining a diphtheria culture of high-toxin producing capacity and growing it so as to yield a strong potent toxin. For antitoxin production on a large scale, healthy horses have been found to serve as the most useful animals. They are then injected subcutaneously (beneath the layers of the skin) with minute and then slowly increasing doses of the diphtheria toxin. The horses gradually become immune, so that it becomes possible to inject larger doses of toxin which if given in like amount at the beginning would have proven fatal. The antitoxin content in the blood of horses injected with diphtheria toxin reach a certain peak and it is not increased even though additional injections of toxin are given. The horse having thus been brought up to a "production basis" is ready for bleedings. The blood, which is collected, is processed to separate the serum, for the latter contains the antitoxic substances or antitoxin. By means of improved methods in the concentration and refinement of the antitoxic blood serum, it is possible to eliminate most of the undesirable albuminous substances and other valueless constituents of the serum. There is then available in a small volume a superior product of high concentration and potency as to its antitoxin value, and low in its content of valueless albumins and solids. The result is that it is easier to administer such a product; there is less pain to the patient and a quicker absorption is the result; and what is of greatest importance is the fact that the rashes and other undesirable effects produced in the

patient and caused by the injection of blood serum (due to the albumins present) are less apt to follow. Not only are the establishments manufacturing diphtheria antitoxin and similar biological products shipped in interstate commerce licensed, their laboratories inspected, and their products tested for purity by the U. S. Public Health Service so as to be assured of the purity of the marketed preparations, but in the case of diphtheria antitoxin, these establishments must record the potency of the latter in terms of "antitoxin units" so as to conform with the uniform standard for measuring the strength furnished by the department at Washington. To explain to a lay audience the exact meaning of "antitoxin units" involves a number of theoretical considerations too difficult to explain briefly. Perhaps as good a non-technical definition as any is that each unit of diphtheria antitoxin represents that amount of antitoxin which will neutralize 100 minimum lethal doses (M. L. D.'s) of freshly prepared diphtheria toxin (definition of M. L. D. of toxin mentioned previously). The marketed diphtheria antitoxins contain not less than from 1000 to 2000 or more of such units to each cc. of contents (a cc. is approximately 15 drops).

USE OF ANTITOXIN

Experimentation and practical clinical observations have revealed as time between the development and absorption of the poison of toxin in the system, and the injection of the antitoxin grows longer, rapidly increasing doses of antitoxin are necessary, and if too much time has elapsed no amount of antitoxin will save. It is therefore apparent that THE EARLIER DIPHTHERIA ANTITOXIN IS ADMINISTERED THE MORE CERTAIN AND RAPID IS THE EFFECT. It has also been found that antitoxin injected beneath the layers of the skin (subcutaneously) is but slowly absorbed. Antitoxin is therefore given intramuscularly in all cases (the gluteal region and the anterior part of the thigh offer suitable sites). In the more severe cases and those in which an insufficient first dose was given or administration was delayed, an additional injection of antitoxin is given intravenously. It is better to give a sufficient and large amount as the first injection than to give many small doses at varying intervals, during the same day. The dosage of diphtheria antitoxin for treatment depends largely upon the severity of the case, its stage of development when seen, and the age of the patient. It may vary from as low as 5000 to 10,000 units in mild cases to from 20,000 to 60,000 units in severe cases. Though diphtheria antitoxin is most valuable for the treatment of diphtheria, it may be employed as a tem-

porary preventive remedy against this scourge. Individuals who have been exposed to diphtheria may be protected from the disease by the administration subcutaneously of 1000 units of antitoxin. This immunity and protection does not last longer than from two to four weeks, so that if it is necessary to prolong the period of protection, injections are to be repeated at least once a month. Where a large number of children or individuals exposed to diphtheria are to be given immediate temporary protection, it is advisable to first determine by the Schick test whether they do or do not possess a natural immunity. All those who are Schick positive and are in danger of contracting the disease are to receive the prophylactic dose of diphtheria antitoxin.

SCHICK REACTION

Studies by many workers have shown that the blood of the majority of normal adults contains naturally a small amount of diphtheria antitoxin. This varying normal antitoxin content probably accounts for the resistance displayed by many individuals to severe infections by the true diphtheria bacilli. In 1913, Bela Schick, formerly of Vienna and now of New York City, presented a simple technique which made possible the detection of this free antitoxin content in individuals.

The Schick reaction is a simple and fairly accurate practical test to determine and separate individuals who do not have naturally in their blood an amount of diphtheria antitoxin sufficient to render them immune to diphtheritic infection. The test can be performed and applied to any person regardless of age. The Schick test has been found eminently satisfactory, and is of especial value and has been used routinely in hospitals, institutions, schools, on large bodies of troops, and among individuals exposed to diphtheria, so as to determine whether it is necessary that such persons should be given immediate protection by administering an immunizing dose of diphtheria antitoxin if they have been exposed to diphtheria; or if there was no exposure whether it is necessary to immunize them for the future with other diphtheria preparations so as to create a more lasting protection. It has been found unnecessary to give prophylactic injections of antitoxin to individuals with a negative Schick reaction (except in the case of young infants). The technique consists in injecting intradermally (intracutaneously) (between the layers of the skin) a minute quantity of the diluted extracellular diphtheria toxin. If the blood of the subject tested contains no diphtheria antitoxin or an amount insufficient for the protection of the individual, a positive tem-

porary, harmless reaction will be apparent in twenty-four to forty-eight hours and may persist for seven to fifteen days. It is at its height in from forty-eight to seventy-two hours when readings are generally made. A control test is always conducted when individuals over five years of age are Schick tested. The control fluid (heated diluted toxin (the heat destroys the toxicity)) is injected in the same manner but in the opposite arm. If the same syringe is used the control fluid is injected first. The explanation of the test is that when no antitoxin is present, the toxin injected acts as a local irritant on the skin, producing a circumscribed area of redness and slight infiltration measuring from 1/3 to 2/3 of an inch in diameter. The absence of a reaction (a negative test due to the fact that the toxin was neutralized) indicates the presence of free antitoxin sufficient to protect the individual against diphtheritic infection (although he may harbor the bacilli as a carrier). The questions, "Is my child susceptible to diphtheria?" and "Am I in danger of contracting diphtheria if exposed to it?" are easily answered after performing the Schick test. This test is also of distinct value in determining whether protection has been attained after injections of diphtheria preparations have been given to create an immunity against diphtheritic infection.

DIPHTHERIA PROPHYLAXIS

Diphtheria prevention programs occupy today and should continue to occupy a most prominent place in the health programs of all communities. Everyone and especially every child has the right to demand and receive the benefit of the great advances made by science in the control of this dreaded scourge. There is no law to compel one to receive immunization treatment if such individual is not protected. Children who are the ones to be considered in the main look to their parents for advice and guidance. All parents are most anxious to provide for the welfare of their children and it is to their sense of obligation that science appeals and says: "Don't let diphtheria threaten your child. Any child who does not possess a natural immunity can be protected permanently against this scourge by the application of simple and safe measures. The health department in your community or your family doctor will give you all the necessary information. Your prompt action now may save you money, time, aggravation, an illness serious in its effects on the child, and who knows possibly some lives may be saved which otherwise may be lost. Your duty is to ACT NOW."

In considering artificial immunization against diphtheria, mention should be made of two types of immunity or marked resistance which can be obtained or developed against this infection. Both of these are an acquired immunity and are either ACTIVE or PASSIVE. ACTIVE IMMUNITY is due to the response of the individual's own body cells and tissues reacting and taking an active part to produce the specific immunity. The reaction is similar to that induced by an attack of the disease even though the symptoms of the disease itself are not pronounced or do not appear. In all instances of active immunity, the virus, or toxins, or causative agent of the disease itself, killed or modified, are introduced into the body of the animal. The reaction by the tissues of the latter is not instantaneous, so that active immunity is slow in the sense that it takes a length of time before the immunity is created. On the other hand, active immunity produces a more lasting protection, one which if it does not endure for life lasts at least for several years. The use of modified smallpox virus (so-called smallpox vaccine) creating an immunity against smallpox is an example of acquired active immunity. PASSIVE IMMUNITY, on the other hand, is a protection created in an individual by introducing specific antibodies or protective substances without the body cells of the individual having reacted or contributed to the antibody production. Passive immunity is possible at a moment's notice, and is quickly brought about by the mere introduction of the protecting substances, usually a serum or a preparation from the latter containing antibodies. The use of diphtheria antitoxin in human beings is an example of passive immunity. Antibodies obtained from the serum of an actively immunized animal are passed or transferred to the individual to be protected. The latter plays but a passive part, receiving something possessing prophylactic properties which has been made outside of his body. Passive immunity lasts but for a short period of time as the antibodies are quickly used up. When children or adults have been exposed to diphtheria, they may be given immediate though temporary protection against the disease by the injection of 1000 units of diphtheria antitoxin. The immunity resulting from the latter lasts for a period of from two to four weeks at the utmost. It is therefore apparent that diphtheria antitoxin though of great value in the treatment of diphtheria where a large quantity of antibodies are required quickly to combat the invading extracellular toxins produced by the diphtheria bacilli, this same preparation is unsatisfactory as a

product to employ for the purpose of developing or creating a MORE LASTING or PERMANENT immunity to this scourge. It is for this reason that efforts have been made to find materials which would be safe, would require simplicity in their use, and would possess definite advantages in producing a more lasting immunity. What was wanted was a product and a technique which would be as effective against diphtheria as modified smallpox virus and vaccination are against smallpox. The introduction of satisfactory agents for the production of a more lasting immunity to diphtheria has resulted after a long series of investigations in the presentation of the following products: Diphtheria Toxin-antitoxin (T-A) Mixture; Diphtheria Toxoid-antitoxin Mixture; Diphtheria Toxoid (Anatoxin, Ramon) and Refined Diphtheria Toxoid (Alum Precipitated); and Toxin-antitoxin Floccules or Flocculi and Toxoid-antitoxin Floccules or Flocculi.

T-A MIXTURE

Originally horses used for the production of diphtheria antitoxin were injected with mixtures of diphtheria toxin and diphtheria antitoxin. The dose of the latter was gradually reduced and finally eliminated in later injections. Various workers suggested the use of toxin-antitoxin (T-A) mixture as the injection in children for practical immunization. Emil von Behring was the first to actually use this mixture in 1913 for the immunization of a group of persons against diphtheria. The following year, in 1914, Dr. William H. Park and his co-workers in New York City used toxin-antitoxin in children, they employing only susceptible individuals who were selected by means of the Schick test. Within one year they injected about 10,000 infants, children and adults in ten different institutions so that records of over a period of more than two decades are available. Since these first cases, more than one-half million school children in New York City alone have been immunized against diphtheria.

Toxin-antitoxin Mixture is a sterile, colorless liquid. It is prepared from diphtheria toxin which has been previously aged and standardized, then mixed with diphtheria antitoxin, and finally diluted that the finished preparation contains a fairly large amount of toxin with a very minute quantity of antitoxin. Diphtheria antitoxin employed commonly is prepared from treated horses. The question was raised that if such antitoxin was used in making T-A Mixture, the individual might become sensitized to horse serum to such a degree as to interfere later in life with an injection of any other remedial agent present

in or prepared from horse serum. To remove and eliminate the remote possibility of sensitizing individuals to horse serum, the antitoxin in the T-A Mixture is obtained from the blood of immunized sheep or goats. Neither of these two animals are ever, or due to their size are likely ever to be used for the production of any marketable therapeutic serum. In using diphtheria antitoxin coming from sheep or goats for this product, the possibility of sensitizing to curative serums (prepared from treated horses) does not exist when using T-A Mixture. Active immunization against diphtheria is accomplished by using a dose of 1 cc. of the mixture. Three injections, all of the same strength, are given subcutaneously (beneath the layers of the skin) in the arm (at the insertion of the deltoid) at weekly or bi-weekly intervals. The development of an immunity frequently requires from eight to twelve months before the Schick test becomes negative. It is important that all children receiving T-A Mixture should be Schick tested twelve months after the initial injection. From 10 per cent. to 15 per cent. may still show a positive Schick reaction. Such children require an additional series of three injections and are to be Schick tested several months after the completion of the second, or each additional series of injections to determine whether an immunity has been created.

TOXOID

Diphtheria toxin upon long standing will lose its toxicity but will be found to retain its initial power for neutralizing its specific antitoxin. In other words, there appears to be no relationship between the toxicity of a toxin and its ability to bind, combine and neutralize its specific antitoxin or its ability to stimulate the production of antitoxin (that is retaining its original immunizing power). With this available knowledge different methods are instituted to modify the toxic powers of diphtheria toxin to prepare what is known as Diphtheria Toxoid (or Anatoxin, as it is known in Europe).

Diphtheria Toxoid or Anatoxin on the market today is a detoxified (non-toxic) modification of diphtheria toxin. The conversion of toxin to toxoid is effected by treatment with formaldehyde (or other chemicals) and incubation or exposure to varying periods of time at different temperatures. Toxoids are free of any serum protein which toxin-antitoxin mixture contains because of the presence of the antitoxin. Toxoids are stable in their immunizing powers. It must be noted however that protein from the culture medium (from

which the toxin entering the toxoids originates) is found in toxoids, and slight protein reactions especially in older children and adults are possible in those sensitive to such proteins. In young children (under six years of age), protein reactions attending the use of toxoids are relatively few and unimportant. Diphtheria Toxoid when used for children and adults is generally administered in two doses of 1 cc. each (15 drops), subcutaneously (beneath the layers of the skin), at intervals of three to four weeks. Infants under one year of age receive two injections of only one-half cc. in each dose. In the use of this as well as when all other prophylactic agents are employed to obtain a more lasting immunity to diphtheria, the Schick test and control are to be made three to four months after the last injection, to determine whether protection has been afforded. Toxoid or Anatoxin is replacing the T-A Mixture for immunization, as less injections are needed, the immunity is developed more quickly, and a greater number of Schick positive persons become Schick negative.

REFINED DIPHTHERIA TOXOID (Alum Precipitated)

It has been found that the addition of a small amount of a sterile solution of alum to a toxoid under suitable conditions will produce a complete precipitation. The supernatant fluid which is discarded contains as high as 80 per cent. of the protein in the original toxoid. The precipitate, after being washed, is resuspended in physiological saline solution (containing a preservative) and is marketed as indicated above. This product, an alum precipitate of diphtheria toxoid in a highly purified state (free of serum albumin and of most of the albumin protein contained in the original toxoid), is administered in single dose treatment subcutaneously or intramuscularly. A Schick test is made two months after the injection. This insoluble suspension will be absorbed but slowly, and the patient should be informed that a nodule or lump will appear after the injection and remain for several weeks. Not only is the pain of injection and reactions reduced to a minimum by this process of refinement, but present indications point to the fact that the degree of immunity secured from a single dose of Alum Precipitated Toxin is higher than that secured from two doses of plain Toxoid or three doses of T-A Mixture.

FLOCCULES OR FLOCCULI

When toxin and antitoxin are mixed together in proportionate amounts to effect a neutralization, a precipitate is formed. A similar reaction will not develop with an excess or too small an amount of antitoxin. The

reaction producing precipitation can be greatly hastened if the test tubes containing such mixtures are placed in a water bath at a temperature of 50° C. to 55° C. It was also observed that flocculi are obtained from precipitation when toxoid and antitoxin are mixed together. Such flocculi had the added advantage of doing away with the possible danger of the mixture becoming toxic. The immunizing value of toxoid-antitoxin flocculi is improved by heating at 80° C. as this temperature destroys the antitoxin. These precipitates or so-called Floccules or Flocculi (Toxin-antitoxin Flocculi or Toxoid-antitoxin flocculi) and even extracts of the latter have been used and are being employed successfully for immunization against diphtheria without producing annoying or objectionable reactions. It is possible that products prepared along these lines may in the very near future be used as the most effective immunizing agents to afford a lasting protection against diphtheria.

WHEN TO IMMUNIZE AGAINST DIPHTHERIA

Age has long been recognized as an important factor and contributing influence to the contracting of diphtheria. It appears that newborn children are endowed with a certain amount of diphtheria antitoxin in their blood. This immunity in human infants is received from their mothers who if immune (and most adults are) transfer the antitoxin through the placental circulation and later probably during nursing. This transmitted immunity in the newborn may last up to twelve months, soon disappears, and is gradually reacquired naturally from the ages of ten to twelve and later. It is therefore exceptional to find infants of a few weeks suffering with diphtheria, and children during the first six months of life are rarely attacked. The most susceptible period is between the ages of one to ten years. The dangerous period is between the ages of two to six. Most adults possess to some degree a natural immunity.

It must be remembered a child under one year of age and even up to two years of age may give a negative Schick test, for reasons mentioned above. Most of these children when tested at a later period however will give a positive Schick test. After four or five years of age, the reactions at this period of life (whether negative or positive) continue to be the same probably for life. Inasmuch as most children between one and six years of age yield positive Schick reactions, this test is generally omitted in practice so that if the young child was intimately exposed to a case of diphtheria, antitoxin is administered for

immediate but temporary protection (passive immunization). Where there has been no exposure but a more lasting immunity is desired, T-A Mixture or Toxoid is administered (active immunization) without conducting the Schick test before the initial injection.

Parents should not delay safeguarding against diphtheria until the child reaches school age. Preschool protection is the best and safest. It is during the first three years of life that the susceptibility to diphtheria as well as the mortality is the greatest. The most suitable age for infants for immunization is six months in the country and nine months in the city or as soon thereafter as convenient. The preferred age of the infants in the country is earlier than in the city as parents in the country are more susceptible and less immune to diphtheria than parents in the city, most of whom are immune. Prompt action at the period of life designated will mean a saving of money, freedom from worry and suffering, and the saving of lives which may otherwise have been lost.

COMPULSORY IMMUNIZATION AGAINST DIPHTHERIA

There are no laws in this country which require nor do health officials compel immunization to diphtheria. However many of the State, County, City and Township Health Departments are providing suitable facilities and even trained physicians for conducting the Schick test and active immunizing treatment, especially in schools and institutions. In their desire to control and eliminate diphtheria, many of these bureaus have arranged to make available immunizing products for all seeking protection against this scourge. All parents owe it to their own sense of obligation and to their desire to provide for the best welfare of their children to apply for and receive approved protective treatment for their babies, infants, and young children.

The Municipal and State Health reports in this and neighboring territories reveal a marked decrease in the number of cases of diphtheria reported during 1934 as compared with previous years. The achievements are due almost wholly to the immunization procedure and to the co-operation of parents with medical practitioners and health and school authorities in an earnest effort to stamp out this disease. It has been clearly established that simple precautions will remove every child from the field of danger, and that universal recognition of this fact will practically eliminate diphtheria as an enemy of humanity. The progress made in all large communities should encourage renewed and continued effort in the cause of child safety, and

everyone should co-operate with their local health authorities in fighting and deliminating this dangerous disease.

A CALL TO ACTION

We have had wonderful discoveries within the past quarter of a century. New remedies have been presented which made possible a prolongation of life and a reduction of suffering. Yet as useful as remedies employed in treating disease may be in adding years of life and in making life happier, they are still less valuable than products which have proven their worth in preventing devastating scourges. We have today insulin which is decreasing the number of deaths of diabetics and in prolonging the lives of the latter, aiding generally in increasing the duration of life. Without underestimating its value, it must be remembered however that insulin therapy has no influence on the incidence of diabetes. It is more significant and of greater importance to make available methods and remedies which will reduce the incidence of disease or completely eradicate scourges, than having in our possession remedial measures and agents to be employed in treating affections which are allowed to develop. The preparations and methods employed to prevent diphtheria are more valuable to mankind than the preparations and methods used in treating this dreaded infection. If the effort is vigorous enough and the resources are adequate for the job on hand, smallpox and diphtheria can be eradicated from the United States and the people in this country can be protected from these disasters.

It is an accepted principle that the care of the health of the indigent sick is a community obligation. Federal, State and local public health departments attempt to supply efficient service in the way of satisfactorily administrating the needed cares and health wants. But these authorities are most frequently handicapped either because of a lack of funds or a lack of co-operation and even due to interference in the carrying out of health regulations due to the deplorable ignorance by the people in regard to what co-operation and efficient service really imply. The health care of the well-to-do or those of adequate means who can afford to pay for their needs is organized reasonably well. The large intermediate class consisting of those of moderate means comprises the group who though able to pay for minor medical service cannot finance unaided all health service due to their restricted incomes. It is not within my province here to discuss the complete socialization and regimentation of medicine which

as the so-called "state medicine" is not looked upon with favor by many interests in this country. Some form of Health Insurance on the prepayment insurance principle in various communities in the United States seems however inevitable. But these methods of health care do not provide for preventive measures. The program for the prevention of disease in this country is supported by the government, private philanthropy, industry and private individuals. The Federal government as well as the State and local governments devote but a fraction of one per cent. of their regular budget directly for the prevention of disease. Much of their allotment is restricted to certain particular fields. Private philanthropy is doing in its own way a valuable service, but the sum total of their financial contribution and that of the governmental agencies would involve altogether an expense less than that required for the upkeep of a few battleships. If for the sake of argument we may stretch our imagination and concede that military forces are needed if only for preventive measures against war, then why isn't there consistency in the distribution of governmental funds? The prevention of disease is of greater import or at least as important as the prevention of war. There should be a greater realization of this fact, and in turn governmental expenditures should be remedied so that a more even balance in the allotment of funds will result. The Federal government should take more of a hand in providing such facilities even to the extent of paying for them in the office of the medical attendant of choice along the lines as carried on in the FERA and CWA. They are spending billions on building construction. Among such projects can be included the building of castles of health, for here they can be assured of greater returns.

We must remember that a corollary of and a contributing cause to the appearance of many cases of these scourges in the near future in all parts of the country will be the reduction of appropriations for public health. The budget for the latter was never what it should have been, and now it has been cut below the average reduction in other municipal expenditures. In other words our public health program about which we moderns and those of us in this country boast so loudly (often too loudly) is suffering considerably more as a result of the economic crises than are communities in general. Because scientists interested in health matters do not (in the main) meddle with politics, because parents and the average citizen do not realize the gravity of the situation, and because in many cases public health

workers themselves are helpless in the face of losing their jobs, local budgets have made cuts (even drastic ones) in the health funds out of all proportion to the general budgetary cuts. It is high time that citizens realize this crisis. A call for action is needed. A call to action must be implemented by a statement for what are we to go into action. What is disease prevention; what ought it to be; what can it be made to be? The basic principle is the possession of good health so that life and living may be happier. But individual health is bound up with community health, and in community or public health are comprised the creation of many projects with which we are all familiar and which are the major factors in the science of human welfare. If we are to accomplish worthwhile results on a large scale, it is high time that we recognize the fact that this is not merely a philanthropic or sentimental local job, but it is a national problem of the very first importance socially and economically. In such a plan universal protection against disease by immunization must play a leading role, especially when considering such diseases as smallpox and diphtheria. Immunization on a large scale has the advantage of production economies not possible on a small scale and of integrated planning and checking as against haphazard methods. This means that such efforts must be in the hands of federal governmental agencies in large measures, for private initiative and local governmental agencies (state, municipal, county, township, etc.) frequently mean uncoordinated development. Health as well as other programs collapse most frequently because of their meagerness and a lack of interest as displayed by the inadequacy of their allotted funds. A program of universal immunization against menacing scourges must be financed by the federal government who at the beginning must supply the funds. Federal administration will also make possible adequate systematic control and guidance and by intelligent operation of economic and legislative controls, worthwhile accomplishments will result. No other known investment is likely to pay such large future dividends, and we will approach more quickly the goal which is the maintenance of every individual's highest level of physical and mental fitness.

COMMERCIAL DRUG PLANTINGS IN OREGON*

By Ernst T. Stuhr†

Introduction

THE Pacific northwest should be especially well adapted to the cultivation of many economic and medicinal plants. Probably no other region in America surpasses the combination of equable temperature and optimum rainfall which is so essential for varied plant life. Successful growing of products, however, requires more than favorable climate. Consideration must be given to the selection of proper soil types for each crop; to proper methods of cultivation for maximum yield; to proper methods of harvesting, preservation, and to numerous other factors.

Comparative Statistics of Oregon

Nature has endowed Oregon with varied climates and soils. Geographically, the state is divided by the Cascade range into two divisions, commonly known as Eastern and Western Oregon. Climatologically, the state is sub-divided into six sections: Coast region, Southern Oregon, Willamette Valley, Columbia Basin, Blue Mountain division, and Central Oregon.

Divisions of Oregon

The eastern division (east of the Cascade range) has dry summers and cold winters. The western division (west of the Cascades) has temperate summers and mild winters, with an abundance of rainfall from October to May.

Comparative Statistics of Precipitation and Temperature of the Geographical Sections of the State

The Coast region has an average of 71.41 inches of precipitation yearly; an average temperature of 51.2 degrees. The Willamette Valley has an average yearly precipitation of 45.02 inches with a temperature of 51.8 degrees. Southern Oregon has an average rainfall of

*Plant Science Seminar, Portland, Oregon, meeting, 1935.

†Department of Pharmacology and Pharmacognosy, Oregon State College.

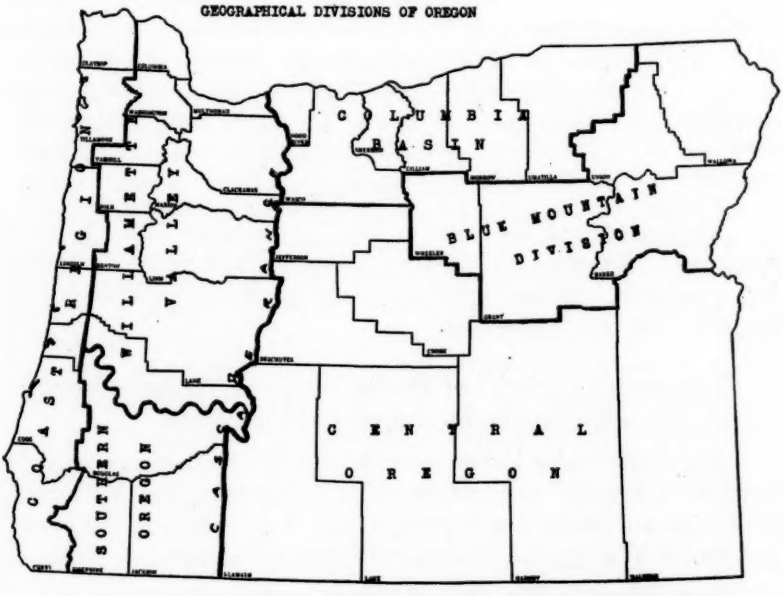
29.83 inches with a temperature of 52.6 degrees; the Columbia Basin has 18.65 inches of rainfall with a temperature of 50.7 degrees; the Blue Mountain region has rainfall of 14.65 inches with a temperature of 48.4 degrees; and Central Oregon has the least amount of rainfall with 11.74 inches yearly and an average temperature of 46.0 degrees. These figures (over a period of thirty years) were computed from the United States Weather Bureau records, and should help in visualizing the climatic conditions—from the very wet to the very dry sections of Oregon. The climate of Western Oregon is the most favorable for varied plant cultivation.

Not only does the western slope of Oregon (and the entire Pacific northwest) have equable temperature and optimal rainfall, but it also has soil fertility probably unsurpassed by any other region in America.

Major Soil Types of Oregon*

In Western Oregon the valley floors are for the most part of dark gray silt loams with black loams in the lower bottom lands and red

SKETCH (MAP)



*"The Oregon Farmer", 1913 Survey, Oregon Experiment Station.

loams in the hills. Eastern Oregon has light silt loams and medium sandy loams in the rolling plains or plateau lands, black silt loams in most valley bottom lands, heavy silt loams in the mountain valleys and red loams in the hill lands. There are light sandy loams on the coast bluffs and coarse sandy loams in the Columbia Basin river bluffs and tributary river bottoms.

Old marsh soils (black "beaver dam") exist in the Willamette Valley, with silty marsh mucks in tideland marshes of the coast and the Columbia River and raw peaty mucks in tideland marshes and Central Oregon interior marshes. There are a few special types of soils like the "adobe", a heavy sticky clay soil, mainly in Southern Oregon, also "granitic", "pumice" and "alkali" soils in some parts of the state.

With the favorable combination of temperature, rainfall and fertility it is not surprising that the area of the Pacific northwest has an impressive display of native flora which is both varied and abundant. In addition, the gardens of the Northwest have been enriched by thriving exotics. Aside from enhancing the beauty of the landscape, the growing season is particularly favorable to diversified cultivation of many economic plants. The development of the natural plant resources of this section is still in the pioneering stage and should prove a worthwhile and profitable undertaking.

There has been a great deal of discussion and many inquiries as to the probabilities of developing the natural plant resources of the Pacific northwest. Many estimates have been made as to the number of economic plants existing in this region. As a result of this popular interest, a comprehensive survey was undertaken by the author and published under the title "Oregon Drug Plants",[1] and a paper "Exploring Economic Plants".[2] These led to the publication of a "Manual of Pacific Coast Drug Plants".[3] The realm of plant life in Oregon, from the mountainous slopes to the fertile valleys is very impressive.

It may be of interest, in this brief description of the 1935 convention state, to consider a few of those native and exotic plants supplying products which enter into the important field of medicine. Their origin and supply make a most interesting story.

REFERENCES

1. *Monograph,* Amer. Phar. Assn., 1931.
2. *Jour. Amer. Phar. Assn.,* Vol. XX, No. 11, 1931.
3. *Science Press,* Lancaster, Pa., 1933.

SURVEY OF COMMERCIAL PROJECTS IN OREGON

County	Crop	Acreage 1932	1933	1934	1935
Benton	Hops		Large acreages		
Clackamas	Celery				50
	Ginseng	30	30	30	30
	Goldenseal	30	30	30	30
	Hops				1000
	Prunes				1500
Clatsop	Ginseng			¼	¼
Columbia	Ginseng			1*	1*
	Peppermint				100
Douglas	Hops			20	20
	Peppermint	20	25	25	25
Hood River	Ginseng	¼	¼	¼	¼
Linn	Cascara	6	8	10	17
	Flax	40	30	25	40
	Ginseng	¼	¼	¼	0
	Goldenseal	¼	¼	¼	0
	Hops				100*
	Peppermint				75*
Malheur	Prunes				400*
Marion	Celery	200	200	200	200
	Flax	10000*	10000*	10000*	10000*
	Ginseng**				
	Hops			5000	5000
	Peppermint		500*	500*	500*
	Prunes	5000	5000	5000	5000
Multnomah	Celery	70	65	65	70
	Fig	8	10	10	10
	Ginseng		½	1	1
	Peppermint				20
	Prunes	45	45	40	40
Polk	Fig	1	1	1	1
	Hops		Large acreages		
	Prunes				10000
Umatilla	Artemisia** (Santonin)				
Yamhill	Flax	600	900	800	700
	Hops	575	800	900	900
	Prunes	6500	6500	6400	6300

*Estimate.

**Small amount.

ESTIMATED COMPARATIVE YEARLY ACREAGES FOR THE STATE

Crop	Years 1932	1933	1934	1935
Artemisia	***	***	***	***
Cascara	6	8	10	17
Celery	270	265	265	320
Figs	9	11	11	11
Flax	10640	10930	10825	10740
Ginseng	30.5	31	32.75	32.5
Goldenseal	30.25	30.25	30.25	30
Hops	17000***	(Plantings doubled)		
Peppermint	***	500	500	695
Prunes	11545***	11545***	11440***	23240

***No definite estimates available at this time.

Possible Projects of Promising Merit

Digitalis

Foxglove, *Digitalis purpurea* L., a native plant, grows abundantly in the coast region. Investigations signify that the commercial cultivation of this native plant should be a promising project.

Berberis

Oregon Grape species abound throughout the mountainous northwest country. Horticulturally it is chiefly used as an ornamental shrub.

Scoparius

Scotch Broom, *Cytisus scoparius* L., and other species are found growing wild along the countryside in Western Oregon. This evergreen shrub is cultivated as an ornamental plant.

Juniper

Found growing wild on the eastern slope of the Cascade range and into eastern and southeastern Oregon counties.

The commercial development of more of the native plants of the Pacific northwest should lead toward a promising future industry, namely, a leading producer of crude drugs and immediate products, for which nature has so splendidly prepared the foundation.

A SOURCE OF ULTRAVIOLET RADIATION AT A COST THAT EVERY PHARMACOGNOSY LABORATORY CAN AFFORD*

By Marin S. Dunn

THE AUTHOR has for some time felt the need of ultraviolet light as one of the tools for the student in the pharmacognosy laboratory, but until recently, owing to the cost of the apparatus necessary, he has been forced to forego its use.

However, this year the difficulty was obviated by the staff of the biology department by copying to some extent the device of Prof. C. C. Pines of the chemical laboratory of P. C. P. & S. The method follows:

At the entrance of the pharmacognosy laboratory is a large display case. A convenient shelf (11 inches deep, 46 inches long and 14 inches high) in this case was selected and fitted with specimen display "set-backs." These in turn were covered with black velvet as were also the side walls. The college electrician wired the under surface of the shelf next above in such a way that there were fourteen standard electrical sockets. In twelve of these were placed General Electric Company's Argon Glow lamps, and the other two outlets (one at each end) were provided with the usual light bulbs. The two ordinary light bulbs work on a conveniently situated switch and furnish ordinary electric light for observation of the specimens. The twelve Argon bulbs may be turned on by a neighboring switch as the ordinary lights are snapped off. The lights and their sockets were enclosed by a blackened metal box except the end facing the shelf covered by the black velvet.

Having done this, a narrow black roller curtain, fitted-to-size, was installed with a window (3 inches wide and 30 inches long) cut at the proper location for easy vision. The curtain is fixed across the front of the case, but may be removed easily by the unfastening of a book. The result was an almost completely enclosed space, with black floor, walls and ceiling, lighted from above by Argon or ordinary bulbs at will. Into this space, specimens were placed for observation through the slit in the shade. A light shield consisting of a piece of hinged wood was fastened to the outside of the case in order to prevent as much daylight as possible from passing from the laboratory into the case through the slit in the curtain.

*Oklahoma meeting of the Plant Science Seminar.

The results, while not as fine as those obtained with expensive ultraviolet lamps, nevertheless are pronounced and sufficiently striking to warrant great student attention and interest.

The following examples give some small idea of the possibilities when using the Argon Glow lamps mentioned above.

1. Rhapontic Rhubarb has a decidedly violet color, and offers a very different appearance from the Chinese.
2. Powdered Hyrastis gives an intense golden yellow color.
3. The acidified liquid from Datura seeds soaked over night in water becomes a vivid green.
4. A glycerine solution in which ipecac has been soaked takes on on a beautiful blue with the U. V. furnished by the Argon bulbs.
5. Petrolatum, especially the crude, displays an unusual fluorescence.

We can accommodate perhaps twenty-five or thirty samples on the shelf at one time. These are placed on black paper, or if in solution, in appropriate containers. Labels are made with a thick aqueous suspension of Hyrastis powder. Among others, we have had excellent results with Berberis, Horse Chestnut, Bloodroot, Split Nux Vomica, and Coptis.

Since the Argon Glow lamps sell at about $0.50 apiece, the total cost, including ordinary lights, velvet, fixtures, wiring, etc., was about ten dollars. Other advantages are the elimination of ozone discomfort, the fact that many students may observe the display at one time in the open laboratory and the cheapness with which replacements and repairs may be made.

Biology Laboratories,
Philadelphia College of Pharmacy and Science.

SCIENTIFIC AND TECHNICAL ABSTRACTS

Compiled by Linwood F. Tice, M. Sc.

Studies on Insulin with Protamine. D. A. Scott and A. M. Fisher. *J. Pharm. and Exper. Therap. 58,* 78 (1936) No. 1. It was recently shown by Hagedorn and his collaborators that when a solution of protamine in sodium phosphate buffer is added to an insulin solution, an insoluble complex forms at pH 7.2 which, when administered to dibetic patients, produces a prolonged hypoglycæmia. Protamine was prepared by Hagedorn and his associates from the rainbow trout. The authors prepared protamine from the testes of salmon by a method described, and a series of experiments with the insulin-protamine combination were performed, the results of which are of considerable interest. Protamine obtained from the salmon gave results practically identical to those obtained with protamine from the rainbow trout. Using protamine and insulin of low ash content, a much less prolonged hypoglycæmia was observed whereas the addition of a small amount of zinc to the insulin before adding the protamine greatly sustained the hypoglycæmic action. These results indicate that zinc, or some other metal, is largely responsible for the combination that results in the prolonged hypoglycæmia produced by insulin with protamine. Further proof of this was shown by the fact that freshly mixed commercial preparations of protamine and insulin (which contained only traces of zinc) are not as effective in prolonging insulin action as are those containing a small amount of added zinc or as suspensions which have stood for forty hours.

The Absorption of Ferrous and Ferric Compounds From the Intestines of Rabbits. O. Fürth and R. Scholl. *J. Pharm. and Exper. Therap. 58,* 14 (1936) No. 1. The absorption of iron preparations is still the subject of acute controversy. One of the most important questions arising from the complicated problem of the oral administration of iron is this: Is there a fundamental difference between absorption and utilization of ferric and ferrous compounds? Since 1926 E. Starkenstein together with his associates have advocated, in a long series of scientific papers, the idea that only ferrous iron is utilized during the clinical treatment of anemia, whereas, ferric iron is

without any effect. Ferrous chloride is claimed to be the most active, whereas ferrous sulfate is not as readily absorbed as ferrous chloride. Therefore the action depends not only on the ferrous cation but also on the nature of the anion. Starkenstein lays great stress on the facts that ferrous compounds unlike ferric compounds do not precipitate proteins, are not caustic, and therefore do not, in proper doses, cause irritation of the gastric and intestinal mucosa.

The authors studied the problem with the view of contributing to an understanding of the complicated and practical problems of iron therapeutics. The absorption of different iron compounds under comparable conditions from ligated intestinal loops of rabbits was investigated, a comparison of the rate of absorption with the toxicity was made, and the rates of diffusion of various iron compounds into gels was compared with their respective rates of absorption from the intestine. The results showed that:

1. The average percentage of iron absorbed in the case of the following compounds of iron were as follows:

Ferrous chloride	61.6
Glutamiron (a ferrous complex)	76.0
Ferrous sulfate	39.7
Ferric chloride	19.8
Iron and ammonium citrate	30.5

2. The absorption of ferrous iron is decidedly impaired by an acid reaction of the intestinal contents.

3. There is no simple interrelationship between the toxicity and the rate of absorption of ferrous and ferric iron from intestinal loops.

4. The speeds of diffusion of ferric and ferrous compounds into gelatin jellies show a certain limited analogy to their rates of absorption.

The Therapeutic Use of Helium. A. L. Barach. *J. A. M. A. 107,* 1273 (1936). Helium has been proposed for therapeutic use in certain types of dyspnea occurring in clinical disease. The basis of its recommendation depends entirely upon its decreased specific gravity in relation to nitrogen. Since nitrogen is about seven times as heavy as helium, a mixture of 21 per cent. oxygen and 79 per cent.

helium provides a mixture comparable to air with only one-third its density. During quiet breathing the influence of such a decrease in weight is practically negligible. However, when there is an obstruction in any part of the respiratory tubal system, an increased negative pressure within the chest becomes necessary for the inward movement of air past the obstruction, and there exists in the passageway between the lung and the site of obstruction a marked increase in pressure of the atmosphere being transported. Furthermore, during violent dyspnea without obstruction in which large volumes of air are moved in and out of the lungs at a high velocity the smaller elements of the respiratory tubal system act as a relative constriction and here too the air is under increased pressure. The function of a helium-oxygen mixture may now be explained by the formula, the velocity of movement of a gas through small orifices is proportional to the square root of the density of the gas. The pressure required for the movement of an 80 per cent. helium-20 per cent. oxygen mixture would be almost one-half that required for air. In human subjects who breathed through narrow orifices an actual reduction as high as 50 per cent. was found in the pressure of a helium-oxygen atmosphere as compared to air. Since pure oxygen is slightly heavier than air, approximately the same reduction in physical force takes place when the helium-oxygen mixture is substituted for pure oxygen. The use of helium-oxygen mixtures in order to reduce respiratory effort has been made in cases of severe asthma or obstructive lesions of the larynx, trachea and bronchi. The clinical application and therapeutic use of helium is described in a series of cases.

The Nomenclature of Estrus Producing Compounds. Report of the Council on Pharmacy and Chemistry. *J. A. M. A. 107,* 1221 (1936). This report reviews the work done by numerous investigators in relation to their contributions to our present understanding of estrus producing substances. Inasmuch as many workers have named the seven known crystalline estrogenic substances in a variety of ways, the importance of an accepted system of nomenclature is obvious. Doisy, following the isolation of the first crystalline estrogenic substance, sought the advice of the Council on Pharmacy and Chemistry on a name for the new compound which would avoid confusion with the many existing commercial names and names for impure extracts. The name selected was theelin and this was approved by the Council.

However, this term was not widely accepted and inasmuch as the root "oestr-" proposed by Adam and his collaborators has been widely adopted among investigators, it was decided by the Council, (1) to adopt the system of nomenclature based on the root "estr"; (2) to retain *theelin, theelol* and *dihydrotheelin* as synonyms for the compounds known in the aforementioned system as *estrone, estriol,* and *estradiol* respectively; and (3) to adopt the term *estrogenic* to describe those compounds or extracts which in addition to their other physiological properties produce estrus and to adopt the noun *estrogen* as the collective term for all the substances having these properties. A table is presented giving the structural, empirical formulas and the common and chemical names of the estrogens.

Limitations of the B. Typhosus Phenol Coefficient as a Measure of the Bactericidal Value of Coal-Tar Disinfestants. E. Klarmann and V. A. Shternov. *J. Ind. Eng. Chem., Anal. Ed. 8,* 369 (1936). Although it has been customary for years to describe the potency of germicides in terms of phenol coefficients, it is not unusual to find that this term is still being used without a complete realization of its significance. It is frequently erroneously assumed that the germicidal effect upon other pathogens corresponds to that upon B. typhosus; i. e., that a disinfectant with a phenol coefficient of 10, for example, is ten times more potent than phenol against all microörganisms. Many investigators have already pointed out the error of such reasoning. The authors investigated the phenol coefficients of various components of disinfectants of coal tar origin both in pure and blended form with the following results: In the case of the pure alkyl-phenol derivatives the germicidal effect upon B. typhosus of the lower homologs parallels that upon other vegetative pathogenic microörganisms. Since cresylic disinfectants contain some lower phenol homologs as the active principle, the same consideration would apply in their case. With the emulsifiable or tar-oil disinfectants, however, there exists no quantitative relationship between the effect upon B. typhosus and that upon other microörganisms; thus some disinfectants of this type with high B. typhosus phenol coefficients may be less effective against other pathogenic microörganisms than those with lower B. typhosus coefficients; or of two products with the same phenol coefficient one may be a better germicide than the other. This condition arises mainly from the indefinite composition of the tar-oil disinfectants and more particularly

from the variations in the ratio of phenolic to nonphenolic constituents. The latter consisting mostly of naphthalene hydrocarbons appear to have a specific effect upon B. typhosus and certain related bacteria, such as B. dysenteriæ, but are much less effective or practically ineffective against other pathogenic microörganisms. The authors recommend the adoption of a supplementary Streptococcus hemolyticus phenol coefficient in order to present a more perfect and complete picture of the germicidal potency of such preparations.

Farming the Sea

Alginates are produced from a species of single-celled brown algæ, or kelp, which grows profusely, often to a length of 200 feet, as a seaweed off the shores of San Diego, California. By refining the kelp, alginic acid of relatively high purity is secured, and from this the various alginic compounds are derived. Established products with which alginates compete include agar and Irish moss, both likewise marine products; tragacanth and karaya, gummy exudations from trees and shrubs; locust-bean gum, obtained by processing the kernels of locust beans, sometimes called St. John's bread; pectin; and gelatine.

Alginates were first commercially introduced in this country during the World War. At that time uniformly pure alginates were not commercially available, and suggestions for the use of alginates were seldom based upon adequate knowledge of their properties. Accordingly those who tried them for their own products were seldom favorably impressed. During the past few years, research and development have resulted in the present commercial production of substantially pure and uniform alginates, and in their use as protective colloid stabilizers in several industries. Research is continuing upon many suggested uses still undeveloped.

The chief present uses for sodium alginates are as stabilizers or anti-settling agents for chocolate milk drinks; as an alternative for gelatine in ice cream; and as a protective colloid or swelling and thickening agent in cosmetics and pharmaceuticals, can-sealing compounds, boiler compounds, etc. Sodium alginate products are now being introduced to the textile industry as a tragacanth substitute in textile printing and padding, and as a gelatine substitute in slasher

sizing. Ammonium alginate is used principally to stabilize rubber latex.

Alginates are produced in various grades, those of greatest hydrating power producing solutions of appreciably greater viscosity than do equal amounts of the chief competing materials. For most of the uses cited, prices tend to be competitive. In the dilutions used, the taste and color of sodium alginates are seldom noticeable, though alginate films, which tend to be softer and more pliable than those of gelatine, are appreciably darker in color. In addition to its use as a source of alginates, kelp is dried and ground to provide organic minerals for foods, medicinal preparations, and stock feeds. Seaweed is likely to achieve increasing importance in industry.

Prophylactic Nasal Spray

SOLUTION A

Trinitrophenol	1 gm.
Normal salt solution	100 cc.

Dissolve with the aid of a gentle heat.

SOLUTION B

Sodium aluminum sulfate	1 gm.
Normal salt solution	100 cc.

Dissolve, and filter.

Mix equal parts of the two liquids.

Because spraying the nose with the above alum-picric acid solution has proved effective in preventing poliomyelitis (infantile paralysis) in monkeys, it is being used on an experimental basis in combating the Alabama-Tennessee epidemic.

Although the U. S. Public Health Service warns that this new development by two of its surgeons, Drs. Charles Armstrong and W. T. Harrison, "is not at present to be regarded as of proved value in the prevention of poliomyelitis in man," directions have been issued telling how the treatment may be administered.

If it is desired to use the solution it should be sprayed into the nostrils three or four times on alternate days, and thereafter weekly during the presence of poliomyelitis. The spray tip should be pointed upward and backward at an angle of about 45 degrees, and the spraying should be thorough enough to reach the pharynx as well, when a bitter taste will be noted.

SOLID EXTRACTS

By Ivor Griffith, Ph. M., Sc. D.

A so-called brand-new product is being offered to kitchens. It is a tendering fluid guaranteed to convert the most leathery part of the rump into a delectable filet mignon.

But there is nothing particularly new about the trick. For centuries, in localities where heat and humidity hasten the rotting of meat and thus forbid the tendering through hanging, freshly killed game is wrapped in fresh papaya leaves (containing a pepsin-like ferment), thus insuring a partly pre-digested game meat. Likewise we are told that gastric juice has been forced into the flesh of freshly killed but antiquated kine, to tenderize their fibers.

Westinghouse also offer an electrical tenderizing system in the shape of a fungicidal ultraviolet lamp.

But if tenderized meat is to be judged by a sample of papaya-tenderized steak recently supplied to us in a certain cafeteria, we shall henceforth order goulash.

"Tiptoe Through the Tulips"—sounds romantic enough until we learn that "tulip fingers" is an affliction much feared by workers in European bulb fields. Symptoms begin twelve hours after handling the bulbs and are characterized by intolerable tingling of the finger-tip beneath the nail, which becomes exquisitely tender; later the nail separates from its bed. The only remedy is to stop handling the bulbs. The testa of the bulb is covered with numerous minute but rigid barbs, which penetrate the finger-tips especially beneath the nail. The acidity of the bulb (pH 4.2, due to phosphoric and oxalic acids) is not responsible, but it has been found that acetic acid develops as a result of fermentation of the maltose of the bulb, and this is capable of producing intense irritation. At one time it was thought that the irritation might be due to bacteria, as antiseptics were found to act as a preventive, but it is now believed that these act by preventing fermentation of the maltose. Constant treatment of the finger-tips with a suitable antiseptic effectively prevents the occurrence of tulip-fingers. Further work by Caulfield (Toronto) shows that the ether-soluble

portion of the bulb is the cause of the dermatitis. Patch tests with ether-extracted bulb material cause severe dermatitis, which it was found could be prevented by intramuscular injections of the ether-soluble fraction in corn oil.

Long before the New Deal used and abused the alphabet in baptizing its projects, the nomenclature of vitamins had exposed the complexity of such alphabetical liberties. Today only an expert remembers what certain of the lesser known vitamin titles really mean. For instance, an English journal refers to vitamin B_9 (pronounce it, and still wonder whether it is benign or not benign).

In any event, since we are for the moment vitamin-minded, it is interesting to note that science now justifies their presence in cosmetics. Of course the spinached smithsters have long since sold their cough drop usefulness. But it is now an accepted fact that vitamin D may be absorbed through the skin even though it may take ten times as much to produce a like result as when the vitamin goes the oral route.

Next month will see the celebration of the centennial of the present patent system of the United States. The Act of 1836, passed on July 4th of that year, inaugurated a regular system of examination of each application before the grant of a patent. The first patent under this act was issued on July 13, 1836, to John Ruggles of Thomaston, Maine, and is number one of the present series, in which current numbers are over 2,054,742 (granted the Amos and Andy Pepsodent). It should not be inferred from this, however, that patent law and procedure is the same now as one hundred years ago, nor that the year 1836 saw the genesis of the patent system in this country.

The first patent law of the Federal Government was passed in 1790, and the first patent thereunder was issued on July 31, 1790, to Samuel Hopkins, for "Making Pot and Pearl Ashes." Even earlier than that, several of the Colonies issued patents. Five years hence will be the three hundredth anniversary of the first of these patents—a grant by the General Court of Massachusetts Bay Colony, in 1641, to Samuel Winslow for making salt. This was called "A treaty with Mr. Winslow touching the making of salt out of meer *salt water."*

The history of patents may be traced still further to a considerably earlier date in England.

Ointment of Sword, or sympathetic salve, was a favorite remedy of the days when the sword was mightier than the pen.

But Oil of Sword is a brand-new, vitamin-rich medication, far ahead of its competitors in life-sustaining elements.

Alive, the swordfish is a big, ferocious, warm-water but not warm-hearted food fish, who will attack and kill a whale, or puncture a boat with his bony nose. A real fighter, his capture is the goal of every deep-sea fisherman who wants one of the greatest thrills this hazardous sport affords. Dead, the swordfish provides the most concentrated natural source of vitamins A and D that we know, swordfish-liver oil, which is sometimes 150 times as rich in these vitamins as good grades of medicinal cod-liver oil. A fisheries company of Gloucester now produces this relatively scarce and valuable oil, new to commerce, which could be used as a vitamin concentrate in itself, and is actually in use for blending with other oils to increase their vitamin content.

"Dirtless farming," "Aquatic agriculture," "Factory farming," terms applied to the new technique of growing enormous crops of vegetables in tanks of water containing the necessary fertilizer chemicals, has now been carried outdoors by its inventor, Prof. W. F. Gericke of the University of California. He has obtained large yields of potatoes (seventy-five tons per acre, according to our informant—to which we say, acres of what?), turnips, carrots, and other garden truck from his outdoor vegetable beds in tanks, and he states that "crops can be grown out of doors in liquid culture medium, in proper season, anywhere the given crop is grown by agriculture.

Professor Gericke started his experiments and achieved his first successes with vegetables and flowers grown under glass—the luxury, out-of-season crops that yield the biggest cash returns. This has worked out so well that now several California greenhousemen are trying the system on a large scale, and the inventor is pioneering with the next step, to bring his tanks out of their glass houses, to test their possibilities in the raising of more plebeian vegetables without the expensive overhead involved in greenhouse culture.

And now the lowly prune aspires to thirst-quenching, head-addling performance, for prune beer is expected to be placed on the market in western States soon.

Eberhard A. Klepper, brewmaster of a large San Francisco brewery, has been granted a patent on a process for the manufacture of prune beer, which he claims has a flavor almost identical with other beers, but a higher vitamin content.

The inventor is now negotiating for the construction of a brewery at Hollister, Calif., in the heart of the prune industry.

Orchardists are watching with considerable interest progress of plans for the manufacture of the new beverage. They state it would open a new outlet for small prunes, always a drug on the market.

When the King of Babylon, whose name is usually spelled Nebuch—etc., became temporarily deranged it is said, in the Bible, that he subsisted on grass, which suggests that he was not so balmy after all. For according to a recent statement all of us may well add to sauerkraut juice, tomato juice, and other juices that are good for what ails us—grass juice.

Drs. C. A. Elvehjem and E. B. Hart of the University of Wisconsin have discovered that the growth-promoting properties of milk can be markedly enhanced by adding fresh grass juice. Juice squeezed out of lawn clippings was added to the daily milk ration of young rats, causing them to gain weight much more rapidly than "control" rats than got just plain milk.

Liver and brain tissue were also found able to promote growth when added to winter milk.

This finding, if it proves applicable to human nutrition, may point to the desirability of fortifying winter milk with materials containing the growth factor which it lacks. Such additions will not be necessary with milk produced in summer, for cows having access to pasture give a product which is potent in promoting growth.

And the stunted soda fountain addict may now add another inch to his stature by asking for a green grass milk shake.

USEFUL SKIN PRESCRIPTIONS

(*The Prescriber*)

The following prescriptions have in most cases been selected from the literature of the past few years as presenting features worthy of notice. They have been carefully revised in accordance with the nomenclature of the British Pharmacopœia (1932) and British Pharmaceutical Codex (1934), and in most cases the metric equivalents are given along with the imperial weights and measures.

CONTACT DERMATITIS

Protective Film

℞

Ivory soap flakes	7.48
Glycerin, pure	26.40
Sodium silicate	24.20
Tragacanth	0.21
Oil of lemon	0.16
Water	41.60

This forms an invisible protective film, soluble in water and non-irritating to the normal skin. Applied to the hands it permits of working with substances likely to cause irritation.

Cook County Hosp.: *J. A. M. A.*, Dec. 21, '35, p. 2064.

FUNGUS INFECTION OF THE FEET

℞

Acidi benzoici	25 gr.	1.6 gm.
Acidi salicylic	15 gr.	1.0 gm.
Paraffini mollis	120 gr.	8.0 gm.
Paraffini duri	15 gr.	1.0 gm.
Olei cocois ..... ad	1 oz.	30.0 gm.

Misce; fiat unguentum. (This is a modification of Ung. Acid. Benz. Co., B. P. C., or Whitfield's ointment.)

℞

Acidi benzoici	90 gr.	6.0 gm.
Acidi salicyli	60 gr.	4.0 gm.
Acetoni	1 fl. oz.	30.0 ml.
Alcoholis ..... ad	4 fl. oz.	120.0 ml.

Misce; fiat pigmentum. (This may be used in place of, or alternated with, the foregoing.)

℞

Cupri nitratis	40 gr.	2.6 gm.
Acidi benzoici	90 gr.	6.0 gm.
Acetoni	1½ fl. oz.	45.0 ml.
Alcoholis	5½ fl. oz.	170.0 ml.
Aquam ad	8 fl. oz.	250.0 ml.

Misce; fiat lotio. Signetur: "Apply twice daily."

M. Sydney Thomson: *Med. Press,* Mar. 4, '36, p. 205.

PRURITUS

℞

Mentholis	4½ gr.	0.5 gm.
Spiritus rectificati	45 m.	5.0 ml.
Talci purificati	2 oz.	100.0 gm.

Misce; fiat pulvis. Signetur: "Use freely as dusting power."

℞

Mentholis	½ gr.	0.015 gm.
Acidi borici	150 gr.	10.000 gm.
Aquae	16 fl. oz.	500.000 ml.

Solve; fiat lotio. Signetur: "Apply on gauze compress."

℞

Mentholis	5 gr.	0.3 gm.
Phenolis	10 gr.	0.6 gm.
Unguenti aquae rosae (B. P. C.)	1 oz.	30.0 gm.

Misce; fiat unguentum. Signetur: "Apply locally as required to prevent scratching."

Cook County Hosp.: *J. A. M. A.,* June 20, '36, p. 2145.

PSORIASIS

℞

Liquoris picis carbonis	60 m.	4.0 ml.
Hydrargyri ammoniati	10 gr.	0.6 gm.
Unguentum paraffini ad	1 oz.	30.0 gm.

Misce; fiat unguentum.

J. A. Drake: *Practitioner,* May '36, pp. 601-602.

RINGWORM OF THE SCALP

℞

Iodine crystals	60 gr.	4.0 gm.
Tri-ethanolamine	60 gr.	4.0 gm.
Goose grease	1 oz.	30.0 gm.

When mixing this prescription do not add the tri-ethanolamine to the iodine, but mix the iodine into the goose grease and then add the tri-ethanolamine with as little friction as possible. The reaction between tri-ethanolamine and iodine is violent, but in the presence of goose grease a slow change takes place. The preparation should be dark brown and should be kept as cold as possible when not in use. When it becomes the color of chicken fat, which takes place in about ten days, the ointment is less effective.

M. T.-R. Maynard: *Arch. Derm. & Syph.,* Aug., '36, p. 268.

PREPARATIONS FOR THE HAIR

The *Pharmaceutical Journal* of November 16, 1935, published an article by Frank Atkins, B.Sc., A.I.C., M.P.S., on "Some New Preparations for the Hair," which included the following formulæ as suitable bases for experiment.

PERMANENT WAVING SOLUTION

Strong liquid ammonia	oz. 2
Borax	oz. 1
Water	to pint 1

Other formulae contain sodium sulphite 10 per cent., potassium bicarbonate and sodium bicarbonate. If a preservative is needed, the usual ones, such as benzoic acid or salicylic acid, are to be avoided in an alkaline medium. Mould formation can be inhibited by the addition of about 0.1 per cent. of Nipagin sodium, a derivative of p-hydroxy benzoic acid.

FRICTION LOTIONS

These usually consist of 70 per cent. alcohol, colored and lightly perfumed. About 1 per cent. of perfume oil is sufficient, but a good quality oil is essential. The spirit content of the lotion must be high.

SETTING LOTION

Powdered Karaya gum	G. 12
Ethylene glycol., or Glycerin	G. 12
Alcohol	Ml. 30 (or less)
Perfume	q. s.

This is to be added to one pint of water, with vigorous shaking. A preservative is necessary, such as salicylic acid, 10 grains to the pint, or methyl p-hydroxy benzoate, 0.1 to 0.15 per cent.

Tragacanth may be used in place of the cheaper karaya gum, but a smaller quantity is necessary about 4 to 8 G., according to its quality. The glycerin in the formula is included to prevent the powdering of the gum on drying. Suitable preservatives are those already given; or formaldehyde may be used.

HAIR FIXATIVES FOR MEN

(a) Non-Oily Type.

A tragacanth mucilage similar to the setting lotion above containing a higher proportion of glycerin (about 10 per cent.) is suitable. The hair is not expected to dry, and the slight stickiness of the extra glycerin is permissible.

(b) Oily Type.

Petroleum jelly	20
Liquid paraffin	8

Color and perfume. The melting point of the mixture should be adjusted to about 38 deg. C. to obtain the best results.

FIXATIVE CREAMS

(a) Water-in-Oil Emulsion Type.

Liquid paraffin	3000
White beeswax	100
Borax	6
Water	150

Usually commercial samples of this type contain 50 per cent. of water, but much skill, experience and an elaborate plant are necessary to produce them.

(b) Oil-in-Water Emulsion Type.

Liquid paraffin	45
Stearic acid	5
Water	49
Triethanolamine	1
Perfume	q. s.

Add the liquid paraffin and stearic acid heated to about 65 deg. C. to the solution of triethanolamine in water at the same temperature, and stir until it thickens. When nearly cold add the perfume. Avoid too vigorous stirring, which causes frothing.

This formula gives a very thick cream, which may be thinned by the addition of water if desired.

Barber's Itch

Thirty or forty years ago barber's itch, or scabies, was very common in the United States. Sometimes half the children in a school would be afflicted. Now the skin ailment is rarely seen in this country, points out the American Institute of Sanitation, saying that its eradication is due to advancing standards of hygiene and the development of efficient disinfecting substances by modern science.

The itch is caused not by germs but by tiny insects, one-fiftieth of an inch in size, burrowing into the skin. Those insects, called mites, tortuously make burrows under the surface of the skin. There they lay eggs, which hatch in about a week. The young mites promptly get to work and bore new subways under the skin, finally emerging on the surface, ready to hop to another person and start a new series of borings. During the Civil War the itch gained a firm foothold among the soldiers because of lack of facilities for personal cleanliness. The ill was then called the "army itch".

"The itch disease is one of the oldest afflictions of man, and is still prevalent in many parts of the Old World where sanitary standards are low. No class has been exempt from its contamination," continues the institute. "Kings have itched as well as peasants.

"The ill is not difficult to overcome. After softening the skin by thorough washing, the tiny bugs and their eggs can be killed by

the common phenolics, chlorine, formaldehyde, and sulfur compounds and other preparations that have been developed during the past quarter of a century.

"Because modern chemical science has developed many highly effective sanitary products, the itch among American soldiers during the World War was kept well under control. There is no longer any excuse for persons to harbor itch mites on their body, bedbugs in their bed, or roaches in the pantry. Such pests are relics of a past civilization, that persist only through indifference."

Soya Statistics

Industrial laboratories are very active in the search for new uses of the products of the soya bean, and, according to the progress announcements, there appears to be no other agricultural products of such wide adaptation. The industrial demand for soya bean is increasing until today it ranks as the fourth largest cash crop to the American farmer. Present indications seem to point that chemical and agricultural research will eventually establish the soya bean as parallel in importance to wheat, corn and oats. The soya bean or its products have already found the following uses:

Paints	Rubber substitutes	Infant diet materials
Varnishes	Floor covering	Meat packing
Plastics	Stock feed	Beverages
Glues	Breakfast cereals	Candy making
Soaps	Flour	
Auto parts	Cooking and salad oil	

The soya bean is a new crop to the farmer, and, because of its varied adaptability, creates markets not heretofore open to agricultural products. It is said to be chemically beneficial to the soil, ideal for crop rotation purposes, and good for silage. There are many types and varieties of the soya bean; hence selection of bean to soil and climate places its cultivation on a national basis. Cultivation has thus far been confined largely to crop production and industrial uses. Selection or breeding of varieties to extended food uses of the soya bean will undoubtedly follow, once the importance of this agricultural product is realized. Nearly one hundred varieties are known and are roughly classified as the "food" and "industrial" types. (A. D. Little, *Industr. Bulletin.*)

BOOK REVIEWS

A Laboratory Manual of Qualitative Chemical Analysis for Students of Pharmacy. By Theodore J. Bradley, Phm. D., A. M., B. S., Dean and Professor of Chemistry in the Massachusetts College of Pharmacy. Fifth edition, revised. Lea & Febiger, Philadelphia, Pa., 1936. 167 Pages. Price $2.25.

This manual is offered only as a guide for laboratory work intended to acquaint the student with the general methods of qualitative analysis and to prepare him to carry out such qualitative tests as the pharmacist may be called upon to make. The course for which this book is a guide is arranged to occupy from four to five hours a week during one school year.

For purposes of identification the metals are classified into the customary seven analytical groups. The analysis of each group is considered in separate chapters and at the end of each chapter there is given a chart for the identification of the elements of all of the preceding groups.

For identification of acids, a division into three groups is made as follows: A. Acids precipitated by silver nitrate; B. Acids precipitated by barium chloride; C. Acids not precipitated in groups A and B. Tables giving the identification tests for these acids in the presence of metals are included, the most valuable of these tables being that for the analysis of a solution for the important metals and acids.

A short chapter on the qualitative analysis of a solid, another including the identity and purity tests for a number of U. S. P. chemicals, and others describing methods for destroying organic matter, general qualitative tests of the U. S. P., and reagents and test solutions, respectively, are also included.

In the opinion of the reviewer the manual is an excellent laboratory guide although, as the author states, "it is in no sense a reference book . . ." and cannot be used as a text or reference for studying the theoretical aspects of qualitative analysis.

Arthur Osol.

A Text Book of Inorganic Pharmceutical Chemistry for Students of Pharmacy and Pharmacists. By Charles H. Rogers, D. Sc. (in Pharm.), Dean of the College of Pharmacy and Professor of Pharmaceutical Chemistry at the University of Minnesota. Second edition, revised. Lea & Febiger, Philadelphia, Pa., 1936. 724 pages, 55 illustrations. Price, $7.00.

The subject matter of this text-book has been formulated and arranged especially for students of pharmacy who have a foundation in general inorganic and qualitative chemistry. As stated by the author in the preface to the first edition of this valuable work, an attempt is made "to present the elements and their compounds in such a manner as to make them interesting to pharmacists and students of pharmacy; to make available the physical constants of inorganic compounds of pharmaceutical importance; to consider collectively the chemistry of the elements and their compounds, the pharmacological actions of the various ions and pharmaceutical preparations; and to include in these considerations any other information of professional interest." And in this attempt the author has more than accomplished his purpose.

In general the elements and their compounds are considered in the order in which they occur in natural groups or families. Their history, occurrence, physical properties, chemical properties, commercial methods of manufacture, laboratory methods of preparation, tests for identity, assay, pharmaceutical preparations and uses, and pharmacological action (if the compound is used medicinally) are interestingly and adequately described under these headings.

In this revised work cognizance has been taken of the advances in pharmaceutical science and of the changes in commercial manufacturing methods. The apparatus used in many of the manufacturing operations is diagrammatically represented.

The reviewer is of the opinion that the book is well adapted for use as a text-book by the student and as a reference work by the pharmacist.

Arthur Osol.